APPENDIX B
U.S. Appl. Ser. No. 09/742,454
Claims as Pending After Entry of the Instant Amendment

39. (Amended) A method of inhibiting the binding of TWEAK to a TWEAK receptor in a mammal in need of such treatment, comprising administering to the mammal an inhibition-effective amount of a composition comprising a TWEAK receptor antagonist wherein the antagonist is selected from the group consisting of a soluble TWEAK receptor polypeptide that binds TWEAK, an antibody that binds the TWEAK receptor, an antisense nucleic acid, a triple helix forming nucleic acid, a peptide, and a small molecule.

46. (New) A method of inhibiting angiogenesis in a mammal in need of such treatment comprising administering a therapeutically-effective amount of a composition comprising an antagonist of a TWEAK receptor, wherein the TWEAK receptor comprises a sequence as set forth from amino acids 28-79 of SEQ ID NO:7.

47. (New) The method of claim 46 wherein the composition further comprises a pharmaceutically acceptable carrier.

48. (New) The method of claim 46 wherein the mammal is a human.

49. (New) The method of claim 46 wherein the mammal has a disease or condition mediated by angiogenesis.

50. (New) The method of claim 49 wherein the disease or condition is characterized by ocular neovascularization.

51. (New) The method of claim 49 wherein the disease or condition is a malignant or metastatic condition.

52. (New) The method of claim 51 wherein the malignant or metastatic condition is a solid tumor.

53. (New) The method of claim 51 wherein the method further comprises treating the mammal with radiation.

54. (New) The method of claim 51 wherein the method further comprises treating the mammal with a chemotherapeutic agent.

55. (New) The method of claim 54 wherein the chemotherapeutic agent is selected from the group consisting of alkylating agents, antimetabolites, vinca alkaloid, plant-derived chemotherapeutics, nitrosoureas, antitumor antibiotics, antitumor enzymes, topoisomerase inhibitors, platinum analogs, adrenocortical suppressants, hormones, hormone agonists, hormone antagonists, antibodies, immunotherapeutics, blood cell factors, radiotherapeutics, and biological response modifiers.

56. (New) The method of claim 54 wherein the chemotherapeutic agent is selected from the group consisting of cisplatin, cyclophosphamide, mechloretamine, melphalan, bleomycin, carboplatin, fluorouracil, 5-fluorodeoxyuridine, methotrexate, taxol, asparaginase, vincristine, vinblastine, lymphokines, cytokines, interleukins, interferons, alpha interferon, beta interferon, delta interferon, TNF, chlorambucil, busulfan, carmustine, lomustine, semustine, streptozocin, dacarbazine, cytarabine, mercaptopurine, thioguanine, vindesine, etoposide, teniposide, dactinomycin, daunorubicin, doxorubicin, plicamycin, mitomycin, L-asparaginase, hydroxyurea, methylhydrazine, mitotane, tamoxifen, and fluoxymesterone.

57. (New) The method of claim 54 wherein the chemotherapeutic agent is selected from the group consisting of Flt3 ligand, CD40 ligand, interleukin-2, interleukin-12, 4-1BB ligand, anti-4-1BB antibodies, TNF antagonists, TNF receptor antagonists, TRAIL, CD148 agonists, VEGF antagonists, VEGF receptor antagonists, and Tek antagonists.

58. (New) The method of claim 46, wherein the antagonist is selected from the group consisting of a soluble TWEAK receptor polypeptide that binds TWEAK, an antibody that binds a TWEAK receptor, an antisense nucleic acid, a triple helix forming nucleic acid, a peptide, and a small molecule.

59. (New) The method claim 58 wherein the antagonist comprises an antibody that binds specifically to the TWEAK receptor extracellular domain.

60. (New) The method of claim 59, wherein the antibody is selected from the group consisting of a monoclonal antibody, a humanized antibody, a transgenic antibody, and a human antibody.

61. (New) The method of claim 59 wherein the antibody is conjugated to a radioisotope, a plant-derived toxin, a fungus-derived toxin, a bacterial-derived toxin, ricin A, diphtheria toxin, or a chemical poison.

62. (New) The method of claim 59, wherein the mammal has a disease or condition mediated by angiogenesis.

63. (New) The method of claim 62 wherein the disease or condition is characterized by ocular neovascularization.

64. (New) The method of claim 62 wherein the disease or condition is a malignant or metastatic condition.

65. (New) The method of claim 64 wherein the malignant or metastatic condition is a solid tumor.

66. (New) The method of claim 64 wherein the method further comprises treating the mammal with radiation.

67. (New) The method of claim 64 wherein the method further comprises treating the mammal with a chemotherapeutic agent.

68. (New) The method of claim 67 wherein the chemotherapeutic agent is selected from the group consisting of alkylating agents, antimetabolites, vinca alkaloid, plant-derived chemotherapeutics, nitrosoureas, antitumor antibiotics, antitumor enzymes, topoisomerase inhibitors, platinum analogs, adrenocortical

suppressants, hormones, hormone agonists, hormone antagonists, antibodies, immunotherapeutics, blood cell factors, radiotherapeutics, and biological response modifiers.

69. (New) The method of claim 67 wherein the chemotherapeutic agent is selected from the group consisting of cisplatin, cyclophosphamide, mechloretamine, melphalan, bleomycin, carboplatin, fluorouracil, 5-fluorodeoxyuridine, methotrexate, taxol, asparaginase, vincristine, vinblastine, lymphokines, cytokines, interleukins, interferons, alpha interferon, beta interferon, delta interferon, TNF, chlorambucil, busulfan, carmustine, lomustine, semustine, streptozocin, dacarbazine, cytarabine, mercaptopurine, thioguanine, vindesine, etoposide, teniposide, dactinomycin, daunorubicin, doxorubicin, plicamycin, mitomycin, L-asparaginase, hydroxyurea, methylhydrazine, mitotane, tamoxifen, and fluoxymesterone.

70. (New) The method of claim 67 wherein the chemotherapeutic agent is selected from the group consisting of Flt3 ligand, CD40 ligand, interleukin-2, interleukin-12, 4-1BB ligand, anti-4-1BB antibodies, TNF antagonists, TNF receptor antagonists, TRAIL, CD148 agonists, VEGF antagonists, VEGF receptor antagonists, and Tek antagonists.

71. (New) The method of claim 58 wherein the antagonist disrupts the interaction between the TWEAK receptor and a TRAF molecule.

72. (New) A method of inhibiting angiogenesis in a mammal in need of such treatment comprising administering a therapeutically-effective amount of a composition comprising an antagonist of a TWEAK receptor, wherein the TWEAK receptor comprises a sequence as set forth from amino acids 28-79 of SEQ ID NO:7, and the antagonist comprises a polypeptide selected from the group consisting of:

(a) a soluble fragment of the polypeptide shown as SEQ ID NO:2, wherein the fragment binds TWEAK; and

(b) a variant that is at least 80% identical to (a), wherein the variant binds TWEAK.

73. (New) The method of claim 72, wherein the antagonist comprises a soluble fragment of the polypeptide shown as SEQ ID NO:2 and the fragment binds TWEAK.

74. (New) The method of claim 72, wherein the antagonist comprises a variant of a soluble fragment of the polypeptide shown in SEQ ID NO:2, the variant is at least 80% identical to the soluble fragment, and the variant binds TWEAK.

75. (New) The method of claim 74 wherein the variant is at least 90% identical to the soluble fragment.

76. (New) The method of claim 75 wherein the variant is at least 98% identical to the soluble fragment.

77. (New) The method of claim 72, wherein the antagonist further comprises an Fc polypeptide, leucine zipper domain, and/or peptide linker.

78. (New) The method of claim 77, wherein the antagonist comprises two to four polypeptides selected from the group consisting of:

(a) a soluble fragment of the polypeptide shown as SEQ ID NO:2, wherein the fragment binds TWEAK; and

(b) a variant that is at least 90% identical to (a), wherein the variant binds TWEAK.

79. (New) The method of claim 77 wherein the antagonist comprises an Fc polypeptide.

80. (New) The method of claim 72 wherein antagonist comprises amino acids 28-79 of SEQ ID NO:7.

81. (New) The method of claim 80 wherein the antagonist comprises amino acids 28-309 of SEQ ID NO:7.

82. (New) The method of claim 72, wherein the mammal has a disease or condition mediated by angiogenesis.

83. (New) The method of claim 82 wherein the disease or condition is characterized by ocular neovascularization.

84. (New) The method of claim 82 wherein the disease or condition is a malignant or metastatic condition.

85. (New) The method of claim 84 wherein the malignant or metastatic condition is a solid tumor.

86. (New) The method of Claim 84 wherein the method further comprises treating the mammal with radiation.

87. (New) The method of claim 84 wherein the method further comprises treating the mammal with a second chemotherapeutic agent.

88. (New) The method of claim 87 wherein the chemotherapeutic agent is selected from the group consisting of alkylating agents, antimetabolites, vinca alkaloid, plant-derived chemotherapeutics, nitrosoureas, antitumor antibiotics, antitumor enzymes, topoisomerase inhibitors, platinum analogs, adrenocortical suppressants, hormones, hormone agonists, hormone antagonists, antibodies, immunotherapeutics, blood cell factors, radiotherapeutics, and biological response modifiers.

89. (New) The method of claim 87 wherein the chemotherapeutic agent is selected from the group consisting of cisplatin, cyclophosphamide, mechloretamine, melphalan, bleomycin, carboplatin, fluorouracil, 5-fluorodeoxyuridine, methotrexate, taxol, asparaginase, vincristine, vinblastine, lymphokines, cytokines, interleukins, interferons, alpha interferon, beta interferon, delta interferon, TNF, chlorambucil, busulfan, carmustine, lomustine, semustine, streptozocin, dacarbazine, cytarabine, mercaptopurine, thioguanine, vindesine, etoposide, teniposide, dactinomycin,

daunorubicin, doxorubicin, plicamycin, mitomycin, L-asparaginase, hydroxyurea, methylhydrazine, mitotane, tamoxifen, and fluoxymesterone.

90. (New) The method of claim 87 wherein the chemotherapeutic agent is selected from the group consisting of Flt3 ligand, CD40 ligand, interleukin-2, interleukin-12, 4-1BB ligand, anti-4-1BB antibodies, TNF antagonists, TNF receptor antagonists, TRAIL, CD148 agonists, VEGF antagonists, VEGF receptor antagonists, and Tek antagonists.Tek antagonists.